REMARKS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

Claims 1 and 9 have been amended significantly, with the support for the amendments being as follows, with reference to the paragraphs of the published application, US 2007/0196479:

1. A method of controlling a computer-controlled dosage device for the controlled dosage of a medicament into a body to be treated as a function of time, comprising the following steps:

a) ~~specifying~~ inputting an indication- and substance-dependant target profile which indicates a desired concentration-time profile or a desired effect-time profile and a dosage time profile which describes the dose administered as a function of time (disclosure [0009] and Fig 1) into a physiology-based and / or pharmacodynamic computer model module (disclosure [0004], Fig. 1),

b) physiology-based pharmacokinetic and/or pharmacodynamic simulating with a time-variable application profile while taking into account individual anatomical, physiological and/or genetic parameters of the body to be treated and substance-specific input parameters of the medicament to be administered within the physiology-based and / or pharmacodynamic computer model module (Fig. 1) and outputting a simulated time profile,

c) iterative numerical adapting of the ~~application~~ dosage time profile until the simulated time profile matches the predetermined target profile and

d) outputting of the dosage time profile on the basis of the result in c) and controlling of ~~a~~ the dosage device according to the dosage time profile ~~on the basis of the result in c)~~.

9. The method of claim 4 wherein one or more of the anatomical, physiological and / or genetic parameters are measured in real-time during the application and integrated as additional input

quantities into the physiology-based and / or pharmacodynamic computer model module (disclosure in [0024]).

Applicants do not believe that any of the amendments introduce new matter. An early notice to that effect is earnestly solicited.

The disclosure was objected to as containing an embedded hyperlink on page 1. In response, Applicants have deleted the hyperlink.

Claims 1-10 were rejected under 35 USC § 101 as claiming non-statutory subject matter. In response, Applicants have amended claim 1, as indicated above, in a manner that clearly intimately ties the inventive method to a machine, and not merely as a minor post-activity solution.

Claims 1-10 were rejected under 35 USC § 112, second paragraph, as being indefinite. In response, Applicants have amended the claims in a manner that Applicants believe overcomes each of the Examiner's concerns.

Claim 1 now recites *"**a** body of a patient to be treated."*

The amendment to claim 1, i.e., that the method is "for the controlled dosage of a medicament ***into a body of a patient*** to be treated" provides antecedent basis for the "humans or animals" recited in claim 2.

In claims 4 and 5, the parenthetical expressions have been deleted.

Finally, in claim 10, "therapy" has been replaced by -- method --.

Claims 1-4 and 7-10 were rejected under 35 USC § 103(a) as being obvious over Christopherson et al. ("Christopherson"), US 5,944,680, in view of Winokur et al. ("Winokur"),

US 5,968,932, in view of Willmann et al. ("Willmann"), *Biosilico, 1:* 121-124 (2003). In response, Applicants respectfully submit that the combination of Christopherson, Winokur and Willmann fails to make out a *prima facie* case of the obviousness of any of the rejected claims. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

First, the Examiner evidently considers Christopherson to be the closest state of the art. However, Applicants strongly disagree with this.

Christopherson describes an implantable stimulation system for computer-controlled delivery of voltage doses in case of abnormal respiratory profile, wherein a stimulation system is programmed to deliver voltage doses so that a disease respiratory profile detected by a sensor is corrected into a target respiratory profile. All programmable parameters mentioned with respect to the detection algorithm and also the stimulus pulse amplitude, duration frequency, on/off times can be adjusted through the physician programmer [col. 33, l. 10-15]. Alternatively, buttons allow the patient to control other parameters such as pulse rate, pulse width, delay times [col. 33, l. 34-37]. In other words, the device of Christopherson detects a profile, compares with a target profile and switches voltage on or off if stimulation is needed; it does not deal with time dosage in the sense of the present invention.

Christopherson also mentions that part of the teaching that is automatic gain control, diagnostic testing, and methods for conserving energy may be applied to other therapy systems including drug delivery systems [col. 6, l. 37 to 41, col 31, l. 21 to 27] but does not give any hint on how in particular diagnostic testing may be applied to drug delivery systems.

Persons skilled in the art would also have been aware that the voltage applied using the implanted device of Christopherson shows immediate effect in the stimulated region whereas the effect of a medicament depends on complex interactions within the treated body, so such persons would not have expected the teaching of the diagnostic testing of Christopherson to be directly applicable to the computer-controlled dosage of a drug without further development.

Applicants respectfully submit that persons skilled in the art may not have considered Christopherson as relevant state of the art for the present invention as drugs and voltage therapy are not comparable.

In particular, such persons would have needed the following questions to be answered:

1. Which of the organ or plasma concentration-time profile is most suitable as a target profile for the yes/no diagnostic test of Christopherson by the drug of interest for example in view of possible critical accumulation?

2. Does the measurable profile have to be converted to be made comparable to the target profile?

Christopherson does not give any answer to these questions.

Applicants also seriously doubt that persons skilled in the art would have considered Christopherson as the closest state of the art to the present invention as such persons would not have considered it a starting point with reasonable chance of success for solving the problem of providing a time dosage profile for computer-controlled delivery of a drug.

These defects in Christopherson are not remedied by Winokur or Willmann alone or in combination.

Winokur describes a drug for the treatment of sleep apnea in various application forms with information of preferred daily doses. Tests were conducted on rats and bulldogs. Winokur is silent about time dosage profile and does not give any hint on how to answer the above mentioned questions.

Willmann teaches the simulation software pK-Sim provides simulated concentration–time profile for all organs in addition to experimental plasma profile [p. 123, last §] depending on application mode and/or characteristics of a subpopulation of patients. Its use in clinical trial is described.

Applicants respectfully submit that persons skilled may have seen in pK-Sim a tool able to provide the target profile as well as a tool for conversion of measured profile required by the diagnostic test of Christopherson adapted to drug delivery. Accordingly, the combination of Christopherson with Winokur and Willmann might have led persons skilled in the art to an application device with the ability to give a yes/no answer to the question of when an application of drug is needed based on the comparison of a measured concentration-time profile with a predetermined target concentration-time profile.

However, the present invention deals with controlling a computer-controlled dosage device for the controlled dosage of a medicament into a body to be treated and calculation of a dosage time profile which is not equivalent to the yes/no decision covered by the diagnostic testing taught by Christopherson.

The Examiner should also note that the method of the invention as defined in claim 1 does not require any measured profile and that the control of the dosage device may be purely

regulated by the pharmacokinetic and/or pharmacodynamic target profile [0024]. Input of measurement signals is the object of one of the particular embodiment described in [0024].

The Examiner should further note that none of the cited reference would have motivated persons skilled in the art to modify the yes/no diagnostic test of Christopherson into a method of controlling a computer-controlled dosage device wherein a dosage time profile is adapted by iterative numerical parameter change until a simulated time profile matches a predetermined target profile for controlling the dosage device according to the dosage time profile, as presently claimed.

In view of the foregoing, Applicants respectfully submit that the combination of Christopherson, Winokur and Willmann does not make out a *prima facie* case of the obviousness of any of the rejected claims. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Claim 5 was rejected under 35 USC § 103(a) as being obvious over Christopherson in view of Winokur in view of Willmann, and further in view of Sugita et al. ("Sugita"), US 2003/0175350. In response, Applicants respectfully submit that this rejection was dependent upon the combination of Christopherson, Winokur and Willmann rendering *prima facie* the broad aspects of the present invention as embodied in main claim 1. Since it has been shown above that this is not, in fact, the case, Applicants respectfully submit that this rejection also should be reconsidered and withdrawn. Indeed, nothing in Sugita overcomes the above-noted defects in Christopherson, Winokur and Willmann. Accordingly, the combination of Christopherson, Winokur, Willmann and Sugita likewise fails to make out a *prima facie* case of the obviousness of claim 5.

Claim 6 was rejected under 35 USC § 103(a) as being obvious over Christopherson in view of Winokur in view of Willmann, and further in view of the definition of "numerical modeling" in *The Dictionary of Physical Geography* (2000). In response, Applicants respectfully submit that this rejection was dependent upon the combination of Christopherson, Winokur and Willmann rendering *prima facie* the broad aspects of the present invention as embodied in main claim 1. Since it has been shown above that this is not, in fact, the case, Applicants respectfully submit that this rejection also should be reconsidered and withdrawn. Indeed, nothing in *The Dictionary of Physical Geography* overcomes the above-noted defects in Christopherson, Winokur and Willmann. Accordingly, the combination of Christopherson, Winokur, Willmann and *The Dictionary of Physical Geography* likewise fails to make out a *prima facie* case of the obviousness of claim 6.

Claims 1, 2, 5, 6, 9 and 10 were provisionally rejected on the ground of obviousness-type double patenting as being unpatentable over claims 2-7 of copending application Serial No. 11/917,452. In response, Applicants note that the rejection is provisional, and reply that the rejection is "provisional" as, indeed, the prosecution is ongoing and the claims here and/or in the related case are subject to change. Accordingly, Applicants respectfully request that this issue be held in abeyance until allowable subject matter is indicated in one of the cases, at which time Applicants will take appropriate action, for example, file a suitable terminal disclaimer or prove patentable distinctness.

Claims 1, 2 and 6 were provisionally rejected on the ground of obviousness-type double patenting as being unpatentable over claims 11, 12 and 16 of copending application Serial No. 11/569,449. In response, Applicants note that the rejection is provisional, and reply that the

rejection is "provisional" as, indeed, the prosecution is ongoing and the claims here and/or in the related case are subject to change. Accordingly, Applicants respectfully request that this issue be held in abeyance until allowable subject matter is indicated in one of the cases, at which time Applicants will take appropriate action, for example, file a suitable terminal disclaimer or prove patentable distinctness.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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